**SUPPLEMENTARY MATERIALS FOR:**

**Manuscript Title**

Differential Molecular Modeling Predictions of Mid and Conventional Dialysate Flows

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**Supplementary Methods – Kinetic Model**

The kinetic models for urea, phosphate and beta2-microglobulin used in our study are all based on a two-compartment model framework that can be described generically with the details for each solute identified subsequently. The general two-compartment model framework used here is very similar to that described by Daugirdas et al for urea kinetics [1], Ward et al for beta2-microglobulin kinetics [2], and Agar et al for phosphate kinetics [3]. The supplementary figure (below) shows the two-compartment model framework schematically. The model assumes that the solute can be considered to be distributed into two separate, well-mixed compartments; 1) a perfused compartment with volume VP from which solute is removed by the dialyzer with a clearance of KD and 2) a non-perfused compartment with volume VNP. The solute concentration in the perfused compartment is denoted as CP and that in the non-perfused compartment as CNP. There is resistance to solute movement between the two compartments; the intercompartment solute mass transfer rate is equal to the product of the intercompartmental clearance (KIC) multiplied by the difference in solute concentration between the two compartments. Solute generation with a rate of G and non-kidney clearance (KNK) was assumed to be confined to the perfused compartment. Fluid is assumed to be removed by the dialyzer at a constant rate QUF from one or both compartments at a constant rate during the dialysis treatment and to be gained by one or both compartments at a constant rate α (a negative value of G) during the interdialytic interval. Residual kidney clearance of all solutes was neglected in this study.

The perfused and non-perfused compartment volumes are different for each solute and are assumed to be approximated by physiological body compartments. For urea, the perfused and non-perfused compartment volumes are assumed to be the extracellular and intracellular fluid volumes, respectively; thus, the sum of the perfused and non-perfused compartments for urea is approximately total body water volume. For beta2-microglobulin, the perfused and non-perfused compartment volumes are assumed to be plasma and interstitial fluid volumes, respectively; thus, the sum of the perfused and non-perfused compartments for beta2-microglobulin is approximately extracellular fluid volume. For phosphate, the perfused compartment volume is assumed to be the extracellular fluid volume and the non-perfused compartment volume is assumed to be infinitely large [3]. For all solutes, fluid is assumed to be removed from the extracellular compartment; thus, fluid is assumed to be removed from the perfused compartment only when considering urea and phosphate, but it is assumed to be removed proportionately from the perfused and non-perfused compartments when considering beta2-microglobulin.

The change in solute mass in the perfused compartment is given by

|  |  |
| --- | --- |
| $$\frac{d(C\_{P}V\_{P})}{dt}=∅\_{P}G+K\_{IC}\left(C\_{NP}-C\_{P}\right)+ϑK\_{D}C\_{P}-K\_{NK}C\_{P}$$ | (1) |

And in the non-perfused compartment by

|  |  |
| --- | --- |
| $$\frac{d\left(C\_{NP}V\_{NP}\right)}{dt}=∅\_{NP}G+K\_{IC}\left(C\_{P}-C\_{NP}\right)$$ | (2) |

In equations (1) and (2), the values of φP and φP denote the fraction of the compartment volumes in the perfused and non-perfused compartments, respectively. The symbol θ is an indicator variable such that θ=1 during an intradialytic interval and θ=0 during an interdialytic interval.

Comparable equations describe the change in volume of the perfused compartment as given by

|  |  |
| --- | --- |
| $$\frac{dV\_{P}}{dt}=-ϑ∅\_{P}Q\_{UF}+\left(1-ϑ\right)∅\_{P}∝$$ | (3) |

and in the non-perfused compartment by

|  |  |
| --- | --- |
| $$\frac{dV\_{NP}}{dt}=-ϑ∅\_{NP}Q\_{UF}+\left(1-ϑ\right)∅\_{NP}∝$$ | (4) |

Note that these equations are those described by Ward et al [2] but neglect the effect of solute transport by convection between the perfused and non-perfused compartments.

To account for solute convection in determining the total dialyzer clearance (KD), we used the following equation for all solutes

|  |  |
| --- | --- |
| $$K\_{D}=K\_{diff}+Tr×Q\_{UF}$$ | (5) |

where Kdiff denotes diffusive solute clearance from the dialyzer as estimated using Michaels’ equation, where the “blood” flow rate term in the equation is the blood water flow rate for urea and plasma flow rate for beta2-microglobulin and phosphate, and Tr denotes the transmittance coefficient [4, 5] defined as

|  |  |
| --- | --- |
| $$Tr=S×(1-\frac{K\_{D}}{Q\_{b}})$$ | (6) |

where the sieving coefficient denoted by S was assumed as 1, 0.8, and 1 for urea, beta2-microglobulin and phosphate, respectively, in this study. When the sieving coefficient is assumed to be unity, the equation for KD reduces to the conventional expression for urea [1].

The values of the various parameters assumed for urea, beta2-microglobulin and phosphate are described in the supplementary table (see below).

**SUPPLEMENTARY TABLE**

|  |  |  |  |
| --- | --- | --- | --- |
| Parameter | For Urea | For beta2-microglobulin | For Phosphate |
| VP | Extracellular Volume (ECV) or TBW/3 | Plasma Volume or ECV/4 | Extracellular Volume or TBW/3 |
| VNP | Intracellular Volume or 2×TBW/3 | Interstitial Tissue Volume or 3 × ECV/4 | Infinitely Large |
| G (mg/min) | Arbitrary | Arbitrary | Neglected |
| KNK (mL/min) | 0 | 3 | 0 |
| φP | 0.33 | 0.25 | 0.33 |
| φNP | 0.67 | 0.75 | 0.67 |
| “Blood Flow Rate” | 0.894 × Qb | 0.67 × Qb | 0.67 × Qb |
| Dialyzer S | 1 | 0.8 | 1 |
| Dialyzer KoA (mL/min) | As reported in main text | 80 [2] | 60% of that for urea |

TBW = Total Body Water Volume and the hematocrit was assumed to be 33%.

**SUPPLEMENTARY FIGURE**

The two-compartment model framework used in this study.



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